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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,797	06/12/2002	Herman Jan Tijmen Coelingh Bennink	97473 US	8680

7590 06/03/2004

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EXAMINER	
KIM, JENNIFER M	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 06/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/031,797	COELINGH BENNINK ET AL.	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,4,10-14 and 16-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,4,10-14 and 16-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/3/2004 has been entered.

Action Summary

The rejection of claims 10 and 11 under 35 U.S.C. 112, second paragraph is hereby expressly withdrawn in view of Applicants' amendment.

The rejection of claims 2,10-14 and 16-18 record under 35. U.S.C. 103(c) being unpatentable over Hodgen of record in view of Schoonen et al. of record and Hamersma et al. of record is being maintained for the reasons stated in the previous office action.

Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hodgen (WO 93/21927) of record in view of Schoonen et al. (XP-002124156) of record and Hamersma et al. (U.S.Patent No. 5,854,235), and further in view of Drug Facts and Comparisons (1997).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2, 10-14 and 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hodgen (WO 93/21927) of record in view of Schoonen et al. (XP-002124156) of record and Hamersma et al. (U.S.Patent No. 5,854,235) of record.

Hodgen teaches a method for minimizing menstrual bleeding irregularities in individuals using progestin-only pharmaceutical preparation, such as contraceptive, comprising administering anti-progesterone such as Org 31710. (abstract, page 5, lines 20-30, page 7, lines 20-32). Hodgen teaches that anti-porgestin above can be administered monthly, or at other intermittent intervals. (page 9, lines 32-36). Hodgen teaches the intervals and number of doses can vary and a suitable regimen is having the anti-progestin administered every thirty days, every sixty days or every ninety days and in the case of contraceptives, the anti-progestin can be administered on the twenty-eighth day of each cycle. (page 10, lines 5-20).

Schoonen teaches the anti-progestinic activity of Org 33245 and Org 33628 are compared to that of Org 31710, in vitro and in vivo, it is shown that both Org 33245 and Org 33628 are more active than the Org 31710. (abstract, page 164, table, right hand column, lines 18-24, page 167, right-hand column, lines 1-7).

Hamersma et al. teach that Org 33245 and Org 33628 are useful in contraception and it exhibit the normal activities known for anti-progestogen such as treatment of menstrual disorders and hormone dependent tumors. (column 1, lines 1-8, column 12, lines 33-36 and lines 43-46).

The differences between Hodgen and Applicants' claims are the employment of specified anti-progestagen, Org 33245 and the sequential non-daily intermittent administration.

It would have been obvious to one of ordinary skill in the art to modify Hodgen's method to employ Org 33245 or Org 33628 in place of Org 31710 because Schoonen teaches both Org 33245 and Org 33628 are compared to that of Org 31710, in vitro and in vivo, it is shown that they are more active than the Org 31710 and because Hemersma et al. teach that both Org 33245 and Org 33628 exhibit the normal activities known for anti-progestogen such as treatment of menstrual disorder and useful for contraception.

One of ordinary skill in the art would have been motivated to modify Hodgen's method to employ either one of Org 33245 or Org 33628 in place of Org 31710 to achieve expected benefit of increased activity of anti-progestin therapy for the contraception and decreased in menstrual disorder such as bleeding. Absent any evidence to contrary, there would have been reasonable expectation of successfully employing Org 33245 or Org 33628 in Hodgen's method in hormone replacement therapy, e.g. contraception and bleeding irregularies. The dosing by sequential non-daily intermittent administration is obvious because the intervals can vary with concurrent medication therapy and each optimum dosing frequency are determined by the practitioners. Moreover, Hodgen teaches that anti-progestin can be administered at other intermittent intervals. (page 9, lines 32-36). One would have been motivated to optimize the intermittent intervals of anti-progestin dosing schedule since other

intermittent intervals can be employed for the anti-progestin therapy as taught by Hodgen et al. There is a lack of teaching in the specification that the sequential non-daily intermittent administration of applicants' anti-progestagen is critical.

Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hodgen (WO 93/21927) of record in view of Schoonen et al. (XP-002124156) of record and Hamersma et al. (U.S.Patent No. 5,854,235) of record as applied to claims 2, 10-14 and 16-18 above, and further in view of Drug Facts and Comparisons (1997).

Hodgen (WO 93/21927) of record, Schoonen et al. (XP-002124156) of record and Hamersma et al. (U.S.Patent No. 5,854,235) as applied as above.

None of references above teaches administration of Org 33245 (anti-progestin) for 1-7, wherein one dosage marks the end of cycle and the optional other dosages are administered regularly divided over the remaining days of the cycle set forth in claim 4.

Drug Facts and Comparisons teaches an antiprogesterone (RU486) are administered once-daily for 7 days are effective abortifacient in early pregnancy and a variety of dosing regimens have been successful. (page 3624, under Clinical trials).

It would have been obvious to one of ordinary skill in the art to employ Org 33245 daily for 1-7 days during a cycle of 28-32 days because it is well known by Drug Facts and Comparisons that antiprogesterone are well-known to be effective and successfully given once-daily for 7 days and a variety of dosing regimens have been successful including intermittent dosage as taught by Hodgen. One would have been motivated to optimize the dosing regimens using 1-7 days therapy employing various known

regimens of intermittent administration with dosage marks to help keep in track of days without surprising and unexpected result.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

None of the claims are allowed.

Response to Arguments

Applicants' arguments filed 3/3/2004 have been fully considered but they are not persuasive. Applicants argue that the Examiner further asserts that the dosing schedule of Applicants' claim 4 is obvious because it was conventional without additional teaching from the art. This is not persuasive because the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the dosing regiment of anti-progestin for the hormonal therapy as contraceptive by administration of 1-7 days and the existence of a variety of successful dosing regimens for anti-progestin for such therapy are well

known by Drug Facts and Comparisons and the intermittent intervals as also known by Hodges. One of ordinary skill in the art would optimize the dosing regimen of Org 33245 for the hormonal therapy of anti-progestin to achieve its known therapeutic effect. Applicants next argue that none of the reference cited by the Examiner teach or suggest surprising properties for Org 33245, which can be put to use in the claimed anti-progestogen therapy. This is not persuasive because it is well known that Org 33245 posses the anti-progestinic activity by Schoonen and Hamersma et al. Therefore it would have been obvious to one of ordinary skill in the art to employ well-known anti-progestin (i.e. Org 33245) by administration of various successful dosage regimen taught by prior art. Applicants next argue that Hodgen does not teach or suggest a method of anti-progestogen therapy by sequential non-daily intermittent administration of Org 33245 and at the best the disclosure of Hodgen as a whole provides the skilled person with the understanding that the anti-progestogen is to be given once per treatment cycle (i.e. on the 28^{th} or 30^{th} day of the treatment) and not on a sequential non-daily intermittent basis. This is not persuasive because Hodgen teaches that anti-progestin can be administered at intermittent intervals (page 9, lines 32-36) and because Drug Facts and comparison teaches that anti-progestin can be administered days 1-7 and variety of dosing regimens have been successful. One of ordinary skill in the art would be motivated to optimize the dosing regimen of Org 33245 with variety of dosing regimens including intermittent 1-7 day dosing without surprising and unexpected result. Applicants further argue that the present application demonstrates that Org 33245 is better suited for embodiments of the present invention than Org

33628, even though it would have been expected in the art from the Scoonen et al. teaching, that Org 33628 would be better suited Org 33628 suffers from a drawback particularly associated with intermittent use since it has the short half-life in humans (about 12 hours). This is not persuasive because Applicants have not provided the half-life of Org 33245 and there is no data comparing the non-daily intermittent dosage regimen of Org 33245 and Org 33628 and because Hamersama et al. teach both Org 33245 and Org 33628 are useful as anti-progestin therapy. Furthermore, the half-life of a known compound would be obvious to one of ordinary skill in the art. One of ordinary skill in the art would adjust the intermittent dosage regimen depend on the half-life of a compound without unexpected result. One of ordinary skill in the art would be motivated to employ either one of anti-progestin by variety of dosing regimen without surprising expected result of the specified dosing regimen claimed by Applicants. With respect to Applicants arguments regarding claims 4 as being incorrect, this is address above. With respect to Applicants arguments regarding claim 11 that Applicants do not understand the basis of the remark of the Examiner that 1-7 days during a cycle of 28-32 day administration is obvious since this is within the conventional dosing regimens of contraception, Applicants attention is drawn to Drug Facts and comparison's teaching of anti-progestins administered for 7 days and the intermittent dosage regimen generally taught by Hodgen. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sreenivasan Padmanabhan
Supervisory Examiner
Art Unit 1617

Jmk
May 21, 2004